AWMSG Secretariat Assessment Report – Limited submission

Ursodeoxycholic acid (Ursofalk®) 250 mg hard capsules, 250 mg/5 ml suspension, 500 mg film-coated tablets

Company: Dr Falk Pharma UK Ltd

Licensed indication under consideration:
For the treatment of hepatobiliary disorders associated with cystic fibrosis in children aged 1 month to 18 years.

Marketing authorisation date: 11 November 2014

Comparator(s):

No other licensed treatments are available for this indication. The products considered to be displaced in the budget impact analysis were other ursodeoxycholic acid (UDCA) products.

Limited submission details:

The limited submission criteria were met based on an estimated small difference in cost compared to comparators and an anticipated minimal budgetary impact in NHS Wales.

Clinical effectiveness:

- Clinical experts have advised that off-label UDCA has been used extensively to treat cystic fibrosis-related liver disease (CFLD). UDCA is recommended for this indication in the Standards for the Clinical Care of Children and Adults with cystic fibrosis in the UK.
- Ursofalk® 250 mg/5 ml suspension is the only product licensed for use in children aged one month to six years and clinical experts highlighted that the Ursofalk® suspension would address a need in young children.
- Ursofalk® is the only licensed treatment available for this indication.
- Marketing authorisation for UCDA was granted following a class change for all UCDA products, where all EU companies with a UDCA product were invited to provide evidence of paediatric use for central assessment known as Article 45 procedure.
- The EU licensing authority concluded that treatment of hepatobiliary disorders associated with cystic fibrosis in children aged one month to < 18 years with UDCA is considered effective at a dose of 20 mg/kg/day in 2-3 divided doses with an increase up to 30 mg/kg/day if necessary based on clinical response.
- The EU licensing authority concluded that overall UDCA was safe and well tolerated. The applicant company was requested to monitor dermatological and haematological adverse events in children as part of pharmacovigilance activities.
- The company submitted evidence from ten controlled studies that reported that UDCA therapy led to significant decrease of the serum liver enzymes in comparison to placebo or no treatment.
- The licensing authority concluded the UDCA is able to demonstrate in the short term as well as long-term use (up to 12 years) improvement in serum liver

enzymes, improved hepatic metabolism of essential fatty acids and bile flow in children with cystic fibrosis. There is some evidence suggesting that treatment with UDCA can decrease bile duct proliferation, halt progression of histological damage and even reverse hepatobiliary changes if given at the early stage of cystic fibrosis associated hepatobiliary disorders.

- The licensing body commented that the 2010 Cochrane review, which concluded there was insufficient evidence to justify routine use of UDCA in cystic fibrosis, was based on three trials with small numbers (estimated around 70 children) which used sub-optimal doses of 10-20 mg/kg/day.

Budget impact:

- Prevalence and incidence data were obtained from a recent paper in the Journal of Cystic Fibrosis which estimates 35 patients per year may be eligible for treatment using prevalence figures of 14% of CFLD in Wales of the total cystic fibrosis population (N = 249).
- The budget impact analysis assumes that Ursofalk® will displace all other UDCA products. An average price (based on UDCA products listed in the Monthly Index of Medical Specialities (Destolit® and generic UDCA), was calculated using, an average body weight of 68 kg and a dose of 20mg/kg/day.
- The company estimates a net cost saving of £4,170 annually for all CFLD patients in Wales.
- The company note that in practice the usage of UDCA for the licensed indication is likely to be overestimated due to using the weight of an average 18-year old male for all patients.
- There are uncertainties with the budget impact analysis as the company has assumed there is no Ursofalk® currently used and an average price has been used which is not weighted according to actual usage. This may overestimate the savings reported as some UDCA preparations are less costly than Ursofalk®. However, the overall budgetary impact would remain minimal.
- The cost of Ursofalk® 250 mg/5 ml suspension (£2.15 per 1,000 mg) is higher than the average price for all Ursofalk® formulations (£1.76 per 1,000 mg).

Additional information:

- AWTTC is of the opinion that, if recommended, ursodeoxycholic acid (Ursofalk®) for the indication under consideration may be appropriate for use within NHS Wales prescribed under specialist recommendation.
- The company do not anticipate that ursodeoxycholic acid (Ursofalk®) will be supplied by a home healthcare provider.

Evidence search:

Date of evidence search: 12 and 13 October 2015.
Date of range of evidence search: No date limits were applied to database searches.

AWMSG review

This assessment report will be considered for review every three years.

References are available on request. Please email AWTTC at AWTTC@Wales.nhs.uk for further information.